



## Prescription patterns of Chinese herbal products for patients with fractures in Taiwan: A nationwide population-based study



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### ABSTRACT

**Ethnopharmacological relevance:** Traditional Chinese medicine (TCM) has been used in the treatment of fracture for thousands of years. However, large-scale surveys examining the utilization of Chinese herbal products (CHPs) for treating fractures and their related symptoms are lacking. This study aimed to investigate the prescription patterns of CHPs among patients with fractures in Taiwan.

**Materials and methods:** The TCM usage in patients with fractures was analyzed using a sample of one million individuals randomly selected from the National Health Insurance Research Database who were newly diagnosis with fractures in 2001–2008, with a followed-up period through 2010.

**Results:** We identified 115,327 patients who were newly diagnosed with fractures in the study population. Among them, 4.97% ( $n=5731$ ) adjunctively utilized TCM for fracture treatment. TCM users were mostly young or middle-aged, female, and resided in highly urbanized areas. With regard to the comorbidities of fractures, TCM users had a lower prevalence of coronary artery disease, chronic obstructive lung disease, diabetes mellitus, hypertension and stroke than non-TCM users, except for osteoporosis. Shu-jing-huo-xue-tang was the most frequently prescribed Chinese herbal formula, while Rhizoma Drynariae (Gu-sui-bu) was the most common single herb for patients with fractures. The CHPs were found to cover not only bone healing but also fracture-related symptoms. TCM users had lower medical expenditure for hospitalization for the first six months after incident fractures than non-TCM users ( $1749 \pm 2650$  versus  $2274 \pm 3159$  US dollars,  $p < 0.0001$ ).

**Conclusions:** Our study identified the TCM utilization for patients with fractures in Taiwan. Integration of TCM treatment reduced the medical costs for hospitalization. Further basic research and clinical studies to investigate the mechanism and clinical efficacies of CHPs are warranted.

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### 1. Introduction

Fracture refers to the separation of a bone into two or more pieces. It can be caused by high impact stress, such as traumatic injury. It can also result from certain pathological conditions that weaken the bones, such as osteoporosis (Cooper et al., 2011) and

fragility fractures (Friedman and Mendelson, 2014). Bone fractures inflict significant burdens on public health. They are associated with medial utilization that is directly attributable not only directly to fracture treatment but also indirectly to the related symptoms of fractures (Friedman and Mendelson, 2014). Current treatment of bone fractures includes surgical or non-surgical approaches, the latter referring to pain relief and stabilization awaiting bone healing. Fracture healing is a complex biological and regenerative process that involves acute inflammation, revascularization and calcification, and finally resuming of the bone structure (Marsell and Einhorn, 2011). Although advances in the management of fractures have improved survival rates, subsequent complications remain difficult problems.

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Traditional Chinese medicine (TCM) is widely used in Taiwan. It has been used to treat various diseases such as allergic disorders (Huang et al., 2013; Yen et al., 2015b), endocrine disorders (Yu et al., 2014), infectious diseases (Yen et al., 2015c), dermatologic diseases (Lin et al., 2014), gynecologic diseases (Yen et al., 2015a) and musculoskeletal disorders (Chen et al., 2014). TCM therapeutic approaches for bone fractures include acupuncture/moxibustion, Chinese traumatology therapy, and Chinese herbal remedies, which can accelerate the bone healing (Hsueh and Chiu, 2012; Peng et al., 2010; Wang et al., 2014). Many TCM herbs are used to promote bone healing or prevent bone loss (He et al., 2014; Lee et al., 2014). However, there is a lack of large-scale, population-based, ethnopharmacological analyses examining the prescription patterns of TCM herbal products for fracture patients.

In Taiwan, the National Health Insurance (NHI) program has reimbursed TCM since 1996. Although the broad definition of TCM includes Chinese herbal medicine, proprietary Chinese medicine, acupuncture, moxibustion, manipulation, and Qi management, only the following three major modalities are covered: (1) Chinese herbal products (CHPs) manufactured by GMP-certified pharmaceutical companies (concentrated scientific TCM granules), (2) acupuncture/moxibustion (including acupuncture, moxibustion and cupping therapy) and (3) Chinese traumatology therapy (including manipulative therapy, acupressure, and tuina massage) (Huang et al., 2014b; Yen et al., 2013). All claims data were collected from the National Health Insurance Research Database (NHIRD).

To investigate the prescription patterns of CHPs for fracture patients, we analyzed a randomly sampled cohort of one million beneficiaries from the NHIRD from 2001–2010. This study is important in laying the groundwork for understanding the TCM utilization patterns. It could be regarded as a consensus of TCM formulas/herbs for patients with fractures. The results of this study will provide useful information for further pharmacological investigation or clinical trials.

## 2. Materials and methods

### 2.1. Data source

The National Health Insurance (NHI) program was launched in Taiwan in 1995 and covered 99.89% of Taiwanese residents in 2010 (BoNH, 2010). The NHI program has reimbursed TCM services, including herbal remedies, acupuncture and Chinese traumatology therapy, since 1996. The option of using TCM or Western medicine is dependent on the patients and is not determined by the insurer. Large computerized datasets (NHIRD; <http://nhird.nhri.org.tw/en/>) were provided by the National Health Insurance Administration and are maintained by the National Health Research Institutes, Taiwan. This database contains de-identified information regarding medical care facilities, specialties, gender, birth dates, visit dates, prescriptions, management, costs and diagnosis codes in the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) format. Accordingly, the claims database provides an optimal platform to evaluate the utilization of TCM therapies (Huang et al., 2014b; Yen et al., 2013).

### 2.2. Study population and variables

A flow chart illustrating the selection of the study cohort is shown in Fig. 1. This study was designed as a population-based cohort of one million beneficiaries from the NHIRD to determine the major independent variables for the utilization of TCM by patients with fractures (ICD-9-CM codes 800–829) from January 1, 2001 to December 31, 2008, with a follow-up period through

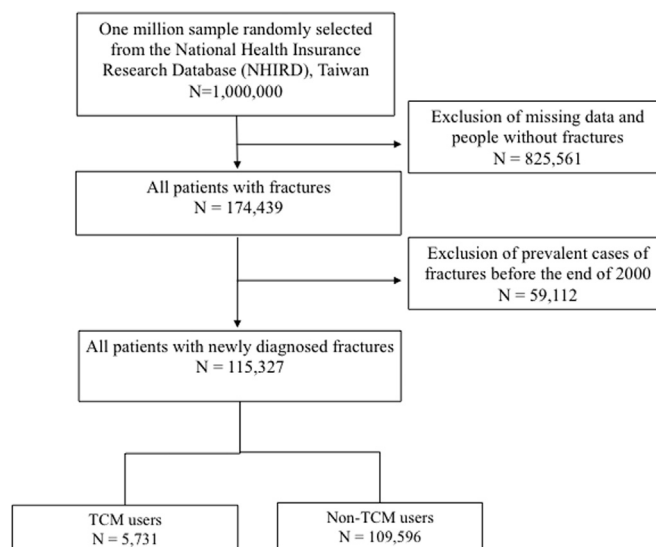


Fig. 1. Flow recruitment chart of subjects from the one million samples randomly selected from the National Health Insurance Research Database (NHIRD) from 2001 to 2010 in Taiwan.

December 31, 2010. A total of 174,439 patients were diagnosed with fractures among the one million beneficiaries. After excluding missing records and prevalent cases, 115,327 of these patients were determined to be newly diagnosed with fractures. As there is no TCM hospitalization service, the utilization of TCM therapies focuses on outpatient services. TCM users ( $n=5731$ , 4.97%) were defined as the patients who visited TCM outpatient services due to fractures or associated problems after a fracture occurred, while non-TCM users ( $n=109,596$ , 95.03%) visited only Western medical doctors. All participants were followed through December 31, 2010. The demographic characteristics and claims data of this study cohort were analyzed. Therapeutic action and indication for TCM prescription were summarized based on TCM theory (Scheid et al., 2009).

The ages of the participants were categorized into four groups: < 20, 20–39, 40–59 and  $\geq 60$  years. The urbanized residence levels of all individuals were classified into four grades based on a previous study (Liu et al., 2006). Level 1 represents the highest urbanized level, while 4 represents the lowest level. The comorbidities of these fractured patients were identified by ICD-9-CM codes including 410–414 (coronary artery disease; CAD), 496 (chronic obstructive lung disease; COPD), 250 (diabetes mellitus; DM), 401–405 (hypertension), 430–438 (stroke) and 733.0 (osteoporosis). The sites of fractures were categorized by ICD-9-CM codes 800–809 (fractures of the skull, neck and trunk), 810–819 (fractures of upper limbs) and 820–829 (fractures of lower limbs). To measure the medical expenditure of the outpatient care and hospitalization between patients with and without TCM treatment, we further calculate the medical expenditure within six months after fractures.

### 2.3. Ethical considerations

All of the datasets from the NHIRD were encrypted and de-identified to protect enrollee privacy. It was not possible to identify individual patients by any means. The Research Ethics Committee of China Medical University and Hospital approved this study (CMU-REC-101-012).

### 2.4. Statistical analysis

All statistical analyses were performed using SAS software,

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